

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (WITHDRAWN) A protein involved in the virulence of Leishmania, comprising at least one site (Cys-Gly-His-Cys) identical to the potential active site of a protein from the protein disulfide-isomerase family (PDI).
2. (CURRENTLY AMENDED) ~~A Leishmania~~ An isolated or a purified protein involved in the virulence of ~~the parasite~~ a *Leishmania* parasite, comprising at least one site (Cys-Gly-His-Cys) identical to ~~the~~ a potential active site of a protein from ~~the~~ a protein disulfide-isomerase family (PDI), wherein said protein is predominantly expressed in the most virulent isolates of the parasite.
3. (CURRENTLY AMENDED) An isolated or a purified protein according to claim 1 or claim 2, characterized in that it is the LmPDI which is a *Leishmania major* protein disulfide isomerase (LmPDI) protein of ~~Leishmania major~~ *Leishmania major*, with having sequence SEQ ID No: 2, ~~or any functional variant of LmPDI having at least 40% identity, preferably at least 80% identity with LmPDI.~~
4. (WITHDRAWN) A recombinant polypeptide comprising at least one fragment of more than 10 amino acids of a protein according to any one of claims 1 to 3, said recombinant polypeptide being capable of triggering an immunological reaction against an epitope of LmPDI when administered to a human or animal host.
5. (WITHDRAWN) A recombinant polypeptide according to claim 4, characterized in that it is the LmPDI-(His)₆ protein with sequence SEQ ID No: 3.

6. (WITHDRAWN) A fusion protein comprising a recombinant polypeptide according to claim 4, fused with a further polypeptide fragment, said fusion protein being capable of triggering an immunological reaction against an LmPDI epitope when it is administered to a human or animal host.

7. (WITHDRAWN) A recombinant nucleic acid sequence coding for a protein or a polypeptide according to any one of claims 1 to 6.

8. (WITHDRAWN) A nucleic acid sequence according to claim 7, characterized in that it comprises the coding sequence corresponding to nucleotides 241 to 1674 of sequence SEQ ID No: 1, or a fragment of said sequence 100 nucleotides or more in size.

9. (WITHDRAWN) A nucleic acid vector, characterized in that it comprises a nucleic acid sequence according to claim 7 or claim 8.

10. (WITHDRAWN) A vector according to claim 9, characterized in that it is a plasmid, a cosmid, a phage or a virus.

11. (WITHDRAWN) A cultured cell comprising a vector according to claim 9 or claim 10.

12. (WITHDRAWN) A cell according to claim 11, characterized in that it is bacterial strain LmPDI-XL₁ deposited at the Collection Nationale de Culture des Microorganismes [CNCM, the National Collection of Microorganism Cultures], on 31/01/2002 with accession number I-2621.

13. (WITHDRAWN) Use of a nucleic acid probe specifically hybridizing under highly stringent conditions with the nucleic acid sequence of SEQ ID No: 2, to determine the presence or absence of the virulence gene coding for LmPDI in a biological sample.

14. (WITHDRAWN) A nucleotide primer, characterized in that it allows specific amplification of at least a portion of the sequence of SEQ ID No: 1, from cells infected with *Leishmania*, thus allowing the presence or absence of the virulence gene coding LmPDI to be determined in a biological sample.

15. (WITHDRAWN) A purified antibody, specifically recognizing LmPDI.

16. (CURRENTLY AMENDED) An immunogenic composition comprising a protein according to claim 1, 2, 3 or 6 and/or a recombinant polypeptide according to claim 4 or claim 5, and/or a nucleic acid sequence according to claim 7 or claim 8, and/or a vector according to claim 9 or claim 10, and/or a cell according to claim 11, 2, wherein said protein is a polypeptide of at least 10 amino acids and wherein said immunogenic composition ~~being~~ is capable of ~~in vitro~~ in vitro stimulation of the proliferation of mononuclear cells originating from individuals who have come into contact with a ~~Leishmania~~ *Leishmania* parasite.

17. (CANCELED)

18. (CURRENTLY AMENDED) An immunogenic composition according to claim 16 ~~or claim 17~~, having a pharmaceutically acceptable formulation for administration to a human or animal host.

19. (CURRENTLY AMENDED) An immunogenic composition according to claim 16 ~~claims 16 to 18~~, capable of inducing an immune response of the Th1 type when administered to a human or animal host.

20. (CANCELED)

21. (CANCELED)

22. (CURRENTLY AMENDED) An immunogenic ~~and/or vaccinating~~ composition according to ~~any one of claims 16 to 21, claim 16,~~ further comprising an antigen foreign to ~~Leishmania and/or Leishmania~~, a nucleic acid sequence coding for an antigen foreign to ~~Leishmania~~ Leishmania, or an antigen foreign to Leishmania and a nucleic acid sequence coding for an antigen foreign to Leishmania.

23. (WITHDRAWN) A method for screening molecules that are susceptible of inhibiting the growth of *Leishmania major*, comprising a step for evaluating the capacity of said molecules to inhibit the activity of LmPDI.

24. (WITHDRAWN) A screening method according to claim 23, in which the step for evaluating the capacity of a molecule to inhibit the activity of LmPDI is carried out in a test for reactivating scrambled RNase A comprising the following steps: incubating scrambled RNase A in the presence of LmPDI under conditions allowing its reactivation; incubating scrambled RNase A under conditions identical to those allowing its reactivation by LmPDI, the molecule to be tested being added; comparing the results obtained in the absence and in the presence of the test molecule, a fault in the reactivation of RNase A in the presence of the test molecule revealing that said molecule has an LmPDI inhibiting activity.

25. (WITHDRAWN) A screening method according to claim 23 or claim 24, further comprising a test for inhibiting the growth of *Leishmania major* in a liquid medium and if appropriate a test for inhibiting the growth of *Leishmania major* in an experimental murine model of leishmaniasis.

26. (WITHDRAWN) Use of one or more protein disulfide-isomerase (PDI) inhibitors, for the preparation of a pharmaceutical composition intended for prophylaxis, attenuation or treatment of infection with Leishmania.

27. (WITHDRAWN) Use according to claim 26, in which a PDI inhibitor is an anti-PDI or anti-LmPDI antibody, bacitracin, zinc bacitracin, 5,5'-dithiobis(2-nitrobenzoic) acid (DTNB), p-chloromercuribenzenesulfonic acid (pCMBS) or tocinoic acid.

28. (WITHDRAWN) Use according to claim 26 or claim 27, for the preparation of a composition for topical, oral or parenteral administration to a human or animal host.

29. (WITHDRAWN) Use of bacitracin or zinc bacitracin as an inhibitor of the growth of a parasite responsible for leishmaniasis or as an active agent against a leishmaniasis infection.

30. (WITHDRAWN) A pharmaceutical composition intended for the treatment of a leishmaniasis infection, comprising an antibody according to claim 15.

31. (WITHDRAWN) A composition according to claim 30, suitable for topical, oral or parenteral administration.

32. (WITHDRAWN) A pharmaceutical composition intended for the treatment of an infection with Leishmania, containing one or more protein disulfide-isomerase (PDI) inhibitors.

33. (WITHDRAWN) A pharmaceutical composition according to claim 32, containing bacitracin or zinc bacitracin.

34. (WITHDRAWN) An in vitro method for diagnosing an infection by a parasite responsible for leishmaniasis, characterized in that it comprises:

- bringing at least one antibody according to claim 15 into contact with a biological sample from a subject partially infected with a parasite responsible for leishmaniasis under conditions allowing the formation of an immune complex between said antibody and antigenic proteins contained in the sample;
- detecting said complex.

35. (WITHDRAWN) A diagnostic kit for carrying out the method according to claim 34, characterized in that it comprises:

- at least one antibody according to claim 15;
- a medium suitable for forming an immune complex with said antibody;
- reagents allowing the detection of any complexes that are formed;
- control samples, if appropriate.

36. (NEW) An immunogenic composition according to claim 18, capable of inducing an immune response of the Th1 type when administered to a human or animal host.

37. (NEW) An immunogenic composition according to claim 18, further comprising an antigen foreign to *Leishmania*, a nucleic acid sequence coding for an antigen foreign to *Leishmania*, or an antigen foreign to *Leishmania* and a nucleic acid sequence coding for an antigen foreign to *Leishmania*.

38. (NEW) An immunogenic composition according to claim 19, further comprising an antigen foreign to *Leishmania*, a nucleic acid sequence coding for an antigen foreign to *Leishmania*, or an antigen foreign to *Leishmania* and a nucleic acid sequence coding for an antigen foreign to *Leishmania*.

39. (NEW) An immunogenic composition comprising a protein according to claim 3, wherein said protein is a polypeptide of at least 10 amino acids and wherein said immunogenic composition is capable of *in vitro* stimulation of the proliferation of mononuclear cells originating from individuals who have come into contact with a *Leishmania* parasite.

40. (NEW) An immunogenic composition according to claim 39 having a pharmaceutically acceptable formulation for administration to a human or animal host.

41. (NEW) An immunogenic composition according to claim 39, capable of inducing an immune response of the Th1 type when administered to a human or animal host.

42. (NEW) An immunogenic composition according to claim 40, capable of inducing an immune response of the Th1 type when administered to a human or animal host.

43. (NEW) An immunogenic composition according to claim 39, further comprising an antigen foreign to *Leishmania*, a nucleic acid sequence coding for an antigen foreign to *Leishmania*, or an antigen foreign to *Leishmania* and a nucleic acid sequence coding for an antigen foreign to *Leishmania*.

44. (NEW) An immunogenic composition according to claim 40, further comprising an antigen foreign to *Leishmania*, a nucleic acid sequence coding for an antigen foreign to *Leishmania*, or an antigen foreign to *Leishmania* and a nucleic acid sequence coding for an antigen foreign to *Leishmania*.

45. (NEW) An immunogenic composition according to claim 41, further comprising an antigen foreign to *Leishmania*, a nucleic acid sequence coding for an

antigen foreign to *Leishmania*, or an antigen foreign to *Leishmania* and a nucleic acid sequence coding for an antigen foreign to *Leishmania*.

46. (NEW) An isolated or a purified protein which is a functional variant of a *Leishmania major* protein disulfide isomerase (LmPDI) protein of *Leishmania major*, wherein the variant has at least 80% identity with SEQ ID NO: 2 and is capable of complementing LmPDI in an infectivity test carried out with an *L. major* strain in which the LmPDI gene has been deactivated.

47. (NEW) An immunogenic composition comprising a protein according to claim 46, wherein said protein is a polypeptide of at least 10 amino acids and wherein said immunogenic composition is capable of *in vitro* stimulation of the proliferation of mononuclear cells originating from individuals who have come into contact with a *Leishmania* parasite.

48. (NEW) An immunogenic composition according to claim 47 having a pharmaceutically acceptable formulation for administration to a human or animal host.

49. (NEW) An immunogenic composition according to claim 47, capable of inducing an immune response of the Th1 type when administered to a human or animal host.

50. (NEW) An immunogenic composition according to claim 48, capable of inducing an immune response of the Th1 type when administered to a human or animal host.

51. (NEW) An immunogenic composition according to claim 47, further comprising an antigen foreign to *Leishmania*, a nucleic acid sequence coding for an

antigen foreign to *Leishmania*, or an antigen foreign to *Leishmania* and a nucleic acid sequence coding for an antigen foreign to *Leishmania*.

52. (NEW) An immunogenic composition according to claim 48, further comprising an antigen foreign to *Leishmania*, a nucleic acid sequence coding for an antigen foreign to *Leishmania*, or an antigen foreign to *Leishmania* and a nucleic acid sequence coding for an antigen foreign to *Leishmania*.

53. (NEW) An immunogenic composition according to claim 49, further comprising an antigen foreign to *Leishmania*, a nucleic acid sequence coding for an antigen foreign to *Leishmania*, or an antigen foreign to *Leishmania* and a nucleic acid sequence coding for an antigen foreign to *Leishmania*.